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CLINICAL STUDY

Value of neutrophil to lymphocyte and platelet to lymphocyte ratios in pneumonia

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ABSTRACT

PURPOSE: In our study, we aimed to evaluate neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in patients with Community-acquired pneumonia (CAP).

METHODS: This is a retrospective study consisting of 114 patients with CAP and 50 control subjects. Patients with CAP were divided into 2 groups, as inpatient and outpatient.

RESULTS: The main findings of our study were that NLR, PLR and CRP levels were significantly higher in CAP than those in the control group. These biomarkers were also higher in inpatient group than outpatient group, but not statistically significant.

CONCLUSION: To our knowledge, this is the first study which investigated the role of NLR and PLR as inflammatory biomarkers and the difference in inpatients and outpatients with CAP and their correlation with CRP values in children. However, larger prospective studies are needed to establish their utility as a predictor for the presence of CAP *(Tab. 1, Fig. 2, Ref. 9).* Text in PDF *www.elis.sk.*

KEY WORDS: CRP, inflammatory biomarkers, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, pneumonia.

Introduction

Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality in developing countries, and particularly in undeveloped countries (1). According to the prediction by the World Health Organization there are 151.8 million new cases of pneumonia each year in children, more than 95 % of them in developing countries and 13.1 million or 8.7 % of which are severe enough to require hospitalization (2, 3). About 2 million pneumonia deaths occur each year in children mainly in undeveloped countries (4). Although the problem is severe and causes many complications, there is still a little evidence-based data on CAP (5). Biomarkers, in combination with clinic and/or chest radiography, are progressively used to specify patients at risk, to determine the significance of disease and prognosis of CAP, as well as to decide on appropriate antibiotic usage (6). Many biochemical markers have been investigated in patients with CAP such as procalcitonin, C-reactive protein (CRP), tumour necrosis factor (TNF), interleukin 6 (IL-6), soluble urokinase plasminogen activator, soluble thrombomodulin (7). Thus, we require urgently new biomarkers that could help to assess the disease severity and simplify the diagnosis process.

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According to the recent studies, novel inflammatory biomarkers such as neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been proposed as indicators of systemic inflammation and infection (8–11). NLR and PLR are easily measurable laboratory biomarkers affected by both natural immune response and acquired immune response (12, 13). In the literature, it was shown that infective endocarditis, *heart valve diseases*, hypertension, *coronary* artery disease, appendicitis, vestibular neuritis, hepatitis B and C, diabetes mellitus, *thyroid disorders*, hepatic failure and renal insufficiency can affect NLR and PLR (14–17).

In the light of these information we conducted a study to evaluate NLR and PLR, novel inflammatory biomarkers obtained from children with CAP and control groups. The main purposes of our study was to decide 1. whether NLR and PLR can be used as diagnostic biomarkers for CAP, 2. whether NLR and PLR can distinguish inpatient and outpatient with CAP, 3. whether NLR and PLR have a correlation with CRP for the evaluation of CAP.

Materials and methods

The present study was conducted between January 2012 and April 2015 in Aksaz Military Hospital and Marmaris State Hospital. Information about medical history, clinical characteristics, demographics and laboratory results were retrieved from computerized hospital medical records and 114 patients were found to have the diagnosis of CAP. Community-acquired pneumonia is defined as the presence of respiratory symptoms including a fever of 38 °C, purulent sputum, cough, breathing difficulties and abnormal chest radiograph.

Tab. 1. Demographic and clinical characteristics.

Feature	Inpatient (n=36)	Outpatient(n=78)	Control(n=50)	P
Age (months)	60.04±22.70	69.79±27.91	62.00±21.55	NS
Gender (male/female)	23/13	36/42	27/23	NS
WBC ($10^3/mm^3$)	11.86±4.38	11.28±3.32	8.61±4.63	<0.001
Neutrophil ($10^3/mm^3$)	8.30±3.79	8.27±6.22	5.43±2.93	0.002
Lymphocyte ($10^3/mm^3$)	3.16±1.24	3.11±1.04	2.74±1.01	0.015
Platelet ($10^3/mm^3$)	296.14±78.75	304.55±77.98	321.33±64.78	NS
CRP	40.64±25.83	39.85±24.66	6.50±1.69	<0.001
NLR	3.48±1.32	3.10±1.24	2.46±0.56	<0.001
PLR	120.42±37.76	118.68±34.41	105.04±28.56	<0.001

Values are expressed as mean±SD. NS – not significant; WBC – white blood cell; CRP – C-reactive protein; NLR – neutrophil to lymphocyte ratio; PLR – platelet to lymphocyte ratio

Patients with CAP were divided into 2 groups, as inpatient and outpatient. The control group included 50 age and sex matched healthy subjects. Complete blood count parameters were measured by an automatic blood counter (Abbott Cell-Dyne Ruby; IL 60064 USA). NLR and PLR were calculated as the ratio of the neutrophils and platelets to lymphocytes. CRP was measured by turbidimetry (UniCelR DxC 800; Beckman Coulter, Pasadena, California, U.S.A.) from blood samples. Patients with chronic inflammatory disorders, infections except CAP, diabetes mellitus, hypertension, chronic renal or hepatic disease, hematological diseases, inflammatory bowel disease, chronic obstructive pulmonary disease, obstructive sleep apnea, allergic rhinitis, asthma, malnutrition, blood transfusion within the last 3 months, and those who did not undergo a blood analysis were excluded from the study. None of the patients had received steroid therapy or another anti-inflammatory drug. The study protocol was approved by the Medical Ethics Committee of Mugla University and conducted in accordance with the ethical principles described by the Declaration of Helsinki.

Statistical analysis

The data were evaluated using SPSS (Statistical Package for Social Sciences) 21.0 program for Windows. Continuous variables were measured as mean+standard deviation. The normality of the distribution of continuous variables was confirmed by Kolmogorov-Smirnov test. One-way analysis of variance was used to evaluate comparisons between the groups. Post hoc analysis was carried out by Tukey test. Pearson correlation analysis was used to assess the relationships. Receiver-operating characteristic (ROC) curve analysis was used to determine the optimum cut off levels of white blood cell (WBC), NLR, PLR and CRP. A $p < 0.05$ was considered significant.

Results

Our study included 114 patients with CAP (78 outpatient; 36 inpatient) and 50 healthy, age and gender matched control subjects. Male/female ratio of outpatient and inpatient with CAP was 36/42 and 23/13, respectively, while it was 27/23 for the control group. Mean age of outpatient, inpatient and the control group was 69.79 ± 27.91; 60.04 ± 22.70; 62.00 ± 21.55 months, respectively. Male/female ratio and mean age of the patient groups and the control group were both similar ($p > 0.05$). The main clinical and laboratory data of the patient and the control group are summarized in Table 1.

The mean CRP levels of the control, inpatient, and outpatient groups were 6.50 ± 1.69, 40.64 ± 25.83, and 39.85 ± 24.66, respectively ($p < 0.05$). The mean NLR levels of the control, inpatient, and outpatient groups were 2.46 ± 0.56, 3.48 ± 1.32, and 3.10 ± 1.24, respectively ($p < 0.05$). The mean PLR levels of the control, inpatient, and outpatient groups were 105.04 ± 28.56, 120.42 ± 37.76, and 118.68 ± 34.41, respectively ($p < 0.05$). The mean CRP, NLR and PLR levels of inpatient and outpatient groups were significantly higher than the control group ($p < 0.05$). However, there was no statistically significant difference between inpatient and outpatient groups ($p > 0.05$).

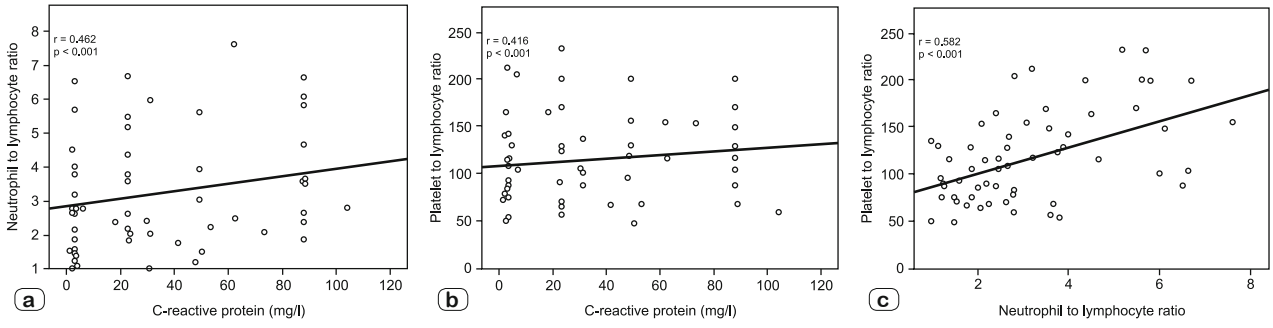

Fig. 1a, 1b, 1c. Correlation analysis showing statistically significant positive correlation between NLR and CRP; PLR and CRP; NLR and PLR.

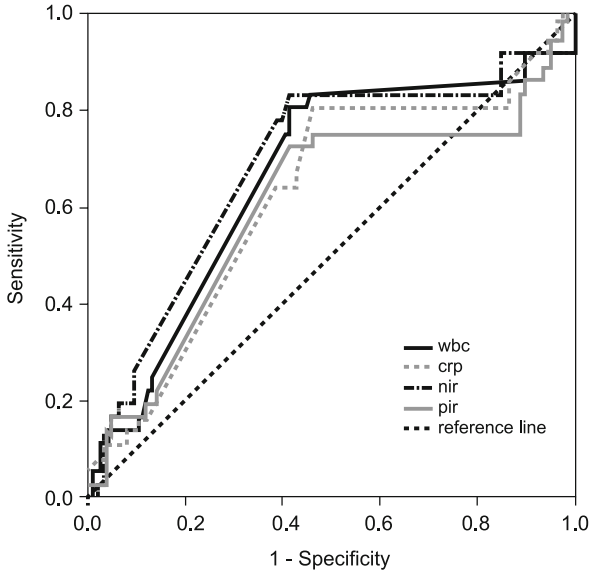

Fig. 2. A plot for comparison of ROC curves among WBC, CRP, NLR, PLR variables. AUC values were found to be 0.66 (0.56–0.77), 0.69 (0.58–0.79), 0.68 (0.49–0.72), 0.63 (0.51–0.73) respectively, and there was no significant difference between any two AUC values (p > 0.05).

Correlation analysis revealed that NLR had a positive correlation with CRP (r = 0.462, p < 0.001) and PLR (r = 0.582, p < 0.001). And also, there was a positive correlation between PLR and CRP (r = 0.416, p < 0.001) (Figs1a,1b, 1c).

A plot for comparison of ROC curves among WBC, CRP, NLR, PLR variables is shown in Figure 2. The *area under the curve* (AUC) values were found to be 0.66 (0.56–0.77), 0.69 (0.58–0.79), 0.68 (0.49–0.72), 0.63 (0.51–0.73) respectively, and there was no significant difference between any two AUC values (p > 0.05). A cut-off value of 20.25 mg/l for CRP was obtained to predict patients with CAP with a sensitivity of 81 % and a specificity of 47 % (p < 0.05). A cut-off value of 2.54 for NLR was obtained to predict patients with CAP with a sensitivity of 83 % and a specificity of 44 % (p < 0.05). A cut-off value of 105.17 for PLR was obtained to predict patients with CAP with a sensitivity of 75 % and a specificity of 46 % (p < 0.05).

Discussion

The main findings of our study were that NLR, PLR and CRP levels were significantly higher in CAP than those in the control group. These biomarkers were also higher in inpatient group than outpatient group, but not statistically significant. NLR and PLR levels were positively correlated with CRP values. To our knowledge, this is the first study which investigated the role of NLR and PLR as inflammatory biomarkers to differentiate inpatient and outpatient with CAP and their correlation with CRP values in children.

Interleukin-6 and TNF, which are involved in the pathogenesis of inflammatory processes, are known to enhance NLR (19–21). Additionally, platelets can influence the different cell types including T-lymphocytes, neutrophils, mononuclear phagocytes, endothelial cells and dendritic cells (22, 23). According to recent studies, activated platelets could trigger the inflammation (22, 23).

Many studies have shown that higher levels of NLR and PLR are associated with increased inflammation such as, in atherosclerosis, myocardial infarction, cystic fibrosis, familial mediterranean fever (FMF), diabetes mellitus, hypertension, metabolic syndrome and coronary artery disease (22–26). O'Brien et al found that NLR has remarkable correlation with clinical conditions in children with cystic fibrosis and children with an NLR≥3 have remarkablely poor lung performance and nutritional condition (27). In another study, Uluca et al showed that NLR is higher in the FMF attack group than in the attack-free FMF patients and healthy control group (28). Additionally, Fu et al evaluated 128 patients with rheumatoid arthritis and 78 healthy individuals and they speculated that NLR and PLR values may be used as potential indices for rheumatoid arthritis disease activity (29). In the present study, our findings are also in accordance with these results.

According to the recent studies, there is a positive correlation between NLR, PLR and CRP. Ahsen et al detected a significantly positive correlation between NLR and CRP in patients with FMF. In this retrospective study, they found that NLR and CRP values of the patients were significantly higher than in the control group (21). The study, which was conducted by Fu et al also showed that NLR and PLR had a significantly positive correlation with CRP (29). In another study, Akboga et al have reported a close relationship between PLR and CRP values. This relationship verified that PLR was independently and positively associated with the severity of coronary atherosclerosis (26). Our results also highlighted a positive correlation between NLR, PLR and CRP.

Limitations of the study

The study has some limitations. First, our study was conducted retrospectively and sample size is relatively small. Second, we just used CRP as an inflammatory marker to establish a connection with NLR and PLR. We didn't use other inflammatory markers. Third, we only used a spot NLR and PLR values for the analysis, rather than follow-up values. Also, we didn't evaluate post-treatment NLR and PLR values.

Conclusion

NLR and PLR are quite simple, inexpensive and easily assessable novel inflammatory biomarkers when compared with other inflammatory markers, such as CRP, procalcitonin, IL-6, TNF and erythrocyte *sedimentation* rate. We found that NLR and PLR were significantly increased in CAP and our findings suggest that they can be used as a predictor for the presence of CAP. However, they are not good inflammatory biomarkers for inpatient or outpatient distinction. Further studies are needed to evaluate this relationship.

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